

## TSRI Center for hESC Research

### Grant Award Details

TSRI Center for hESC Research

**Grant Type:** Shared Labs

**Grant Number:** CL1-00502-1.1

**Investigator:**

**Name:** Sheng Ding

**Institution:** Gladstone Institutes, J. David

**Type:** PI

**Award Value:** \$1,440,164

**Status:** Closed

### Grant Application Details

**Application Title:** Center for hESC Research

**Public Abstract:** The therapeutic use of stem cells in regenerative medicine will require the ability to control stem cell expansion and differentiation into specific tissue types, such as pancreatic  $\beta$ -cells, heart tissue, bone or specific neuronal lineages. We have taken a chemical approach toward this problem in which large collections of synthetic small molecules are being screened in cell-based assays to identify drug-like molecules that control stem cell processes. Preliminary experiments in our institute have demonstrated that we can identify molecules that control the self-renewal and directed differentiation of murine embryonic stem cells. The characterization of the biological mechanisms of the molecules has also provided new insights into the underlying biology of stem cells. We now propose to extend these studies to hESC lines not eligible for federal funding, for which our research activities have been restricted to date. In addition, such lines may be better suited for specific applications, including the use of small molecules to derive specific cell lineages and investigate ES derived cell-based models of genetic disease. To this end, we would like to establish a human embryonic stem cell core facility. This facility will house the necessary equipment to genetically manipulate and culture hESCs on a large scale for a variety of studies including cell-based screens of small molecule libraries, as well as screens of arrayed genomic cDNA and siRNA libraries. We anticipate that this facility will serve our faculty as well as other labs that would like to collaboratively exploit this chemical approach to the study and manipulation of stem cells.

**Statement of Benefit to California:**

Historically, small molecules have been more useful than genetic approaches in the treatment of human disease. However, much of our ability to control embryonic stem cell self-renewal and directed differentiation currently involves genetic manipulation of these cells or complex mixtures of protein factors. The demonstration that one can systematically identify, optimize and characterize the mechanism of action of small drug-like molecules that selectively control stem cell biology both in vitro and in vivo will: (1) provide important tools to manipulate stem cells in the lab; (2) provide new insights into the complex biology that regulates stem cell differentiation; and (3) provide an important first step which may ultimately lead to drugs that facilitate the clinical application of stem cells.

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